

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

Inventor: Robert Kleiman

Docket No. FLORA.1100

Serial No. 09/899,432

Examiner: Shobha Kantamneni

Filing Date: 07/06/2001

Art Unit: 1617

Title: ANTIVIRAL COMPOSITION AND
TREATMENT METHOD

REPLY BRIEF

MAIL STOP: REPLY BRIEF - PATENTS
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VIRGINIA 22313-1450

Dear Commissioner:

This is a reply brief, pursuant to 37 C.F.R. §41.37 (c), in response to the Examiner's Answer dated 11/07/2008, wherein the Examiner maintained her final rejection of claims **91-102** of the present application. The rejected claims were reproduced in the Claims Appendix attached to Appellants' Appeal Brief filed on 07/22/2008, and are re-attached hereto as Appendix A for ease of review.

I. STATUS OF CLAIMS

1. All originally filed claims **1-90** have been cancelled or withdrawn. Specifically, claims **1, 3-4, 6-13, 15, 16, 18-19, 21-22, 24-25, 27-28, 30-31, 33-34, 36-85, 87-88** and **90** have been cancelled. Claims **2, 5, 14, 17, 20, 23, 26, 29, 32, 35, 8** and **89** have been withdrawn. A copy of the claims being appealed, namely **91-102**, are provided in Appendix A. Claims **91-102** were previously presented.
2. Claims **91-92** are rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of PCT Publication No. WO 9920224 to Arquette *et al.*
3. Claims **93-102** are rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of U.S. Patent No. 4,874, 794 to Katz or U.S. Patent No. 5,070,107 to Katz.

II. GROUND OF REJECTION TO BE REVIEWED ON APPEAL

Issue 1:

Whether the Examiner effectively establishes a *prima facie* basis for obviousness under 35 U.S.C. § 103(a) for claims **91-92**; and more specifically, whether claims **91-92** are obvious over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of PCT Publication No. WO 9920224 to Arquette *et al.*

Issue 2:

Whether the Examiner effectively establishes a *prima facie* basis for obviousness under 35 U.S.C. § 103(a) for claims **93-102**; and, more specifically, whether claims **93-102** are obvious over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of U.S. Patent No. 4,874,794 to Katz or U.S. Patent No. 5,070,107 to Katz.

III. ARGUMENT

ISSUE 1: REJECTIONS UNDER §103(a) OF CLAIMS 91-92

Claims 91-92 are rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of PCT Publication No. WO 9920224 to Arquette *et al.* Appellants further submit that a *prima facie* case of obviousness has not been established, as discussed in Appellants' Appeal Brief, pages 13-22.

In response to the arguments made in Appellant's Appeal Brief, the Examiner maintains the cited references teach the following:

Katz *et al.* teaches that long chain fatty acids broadly including oleic acid (C18 one double bond), n-docosanoic acid (C22 acid, see column 3 of '391, lines 9-11) and long chain alcohols such as docosenol, brassidyl alcohol in their effective amounts in a topical pharmaceutical composition are useful in treating viral infection. (Examiner's Answer, page 10).

Arquette teaches that instant fatty acid esters are known to be used as emollients in topical pharmaceutical compositions[...]. (Examiner's Answer, page 10).

Sintov *et al.* teaches that salts of oleic acid are employed in treating viral infection. (Examiner's Answer, page 10).

Claim 91 of the present invention requires *inter alia* "at least one salt of a jojoba-derived trans-free fatty acid according to the formula $R^1\text{-COO}^-\text{M}^+$, wherein: R^1 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_x$; x is at least one of 8, 10, and 12". The Examiner has admitted that none of the cited references of record, or any combination thereof, teach this element of Appellant's claimed invention, either alone or in combination with any of the other elements of Appellant's claimed invention. (See Examiner's Answer, page 5).

In order to overcome this deficiency in the rejection, the Examiner puts forth several arguments, all of which fail for the reasons identified below.

One of ordinary skill in the art at the time of invention would have been motivated to utilize the C20 fatty acid salts as instantly claimed in the method of treating viral infection because of an expectation of success similar to that taught for structurally similar prior art species i.e. C18 acids, and salts, since structurally similar compounds usually have similar properties, and further Katz teaches that long chain fatty acids broadly including oleic acid (C18 one double bond), n-docosanoic acid (C22 acid, see column 3 of '392, lines 9-11) have antiviral activity. One having ordinary skill in the art at the time the invention was made would have been motivated to employ the instant long chain fatty acid salt in combination with long chain alcohols because 1) the instant long chain fatty acid salt (C20 acids) are structurally similar to alkali metal oleate (C18 acid), and will possess similar anti-viral properties as that of alkali metal oleate, and 2) monounsaturated long chain alcohols are known to be useful to treat virus-induced and inflammatory disease of skin and membranes according to Katz et. al. (5,952,392). Accordingly, one of ordinary skill in the art would have been motivated to combine instant long chain fatty acid salt and long chain alcohol with reasonable expectation [of] success of obtaining a pharmaceutical composition for treating virus-induced and inflammatory disease of skin and membranes with at least additive effect. (Examiner's Answer, page 11).

The Examiner provides no objective evidence (and in fact no evidence at all) that the fatty acid salts of Sintov *et al.* are structurally similar. The scope of Sintov *et al.* is properly limited to salts of shorter chain fatty acids. See Sintov *et al.*, page 2 and claim 2. Shorter chain fatty acids, disclosed in Sintov *et al.*, and longer chain fatty acids as required by the present invention, do not have similar structural properties. Specifically, they have different solubility characteristics, which would lead one of ordinary skill in the art to determine that they would have different anti-viral properties. See 37 C.F.R. § 1.132 Affidavit of David Ashley, Exhibit 7 of Appellants' Appeal Brief ("This effect could not have been expected based on the general knowledge available because salts of fatty acids with carbon chain lengths 20 carbons or greater would generally have been thought to hinder adsorption due to their insolubility"). The dramatically improved activity of the *less soluble* salts of longer-chain fatty acids in combination with the alcohols and mixed esters of the claimed invention is surprising, and could not have been expected based on the disclosure of Sintov *et al.*

In the Answer, the Examiner maintains the false distinctions regarding solubility of the fatty acids salts in different solvents before simply concluding that "it has been well-established that consideration of a reference is not limited to the preferred embodiments or working examples,

but extends to the entire disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to [a] person of ordinary skill in the art". (See Examiner's Answer, page 13). However, Sintov *et al.* cannot be viewed to fairly teach C20+ chain fatty acid salts. See Appellant's Brief, 17-20, 37 C.F.R. § 1.132 Affidavit of David Ashley, Exhibit 7 of Appellant's Appeal Brief. Moreover, Appellants submit that the teachings of *In re Dillon* (originally cited by the Examiner for support of the Examiner's position) actually further support Appellants' view of the scope of Sintov *et al.* *In re Dillon* requires both structural and functional similarities in order to bridge the gap between the specific teachings of a reference and the claimed invention. The Examiner has provided no evidence of functional similarity and has done nothing more than discount Appellants' objective evidence of functional dis-similarity. 37 C.F.R. § 1.132 Affidavit of David Ashley, Exhibit 7 of Appellant's Appeal Brief. The Examiner attempts to proffer evidence of structurally similar compounds providing similar properties by citing Katz *et al.* for the proposition that "Katz teaches that long chain fatty acids with a carbon chain length of greater than 20 have antiviral activity". (Examiner's Answer, pages 13-14). There are two deficiencies in the Examiner's reasoning in this regard. First, Katz does not teach salts of fatty acids at all, and therefore Appellant is affirmatively unaware as to how purported salts of shorter chain fatty acids can be deemed "structurally similar" to longer chain fatty acids in view of Katz, either taken alone or in combination with Sintov *et al.* Indeed, the Examiner provides no such explanation to bridge this gap.

The fact remains that the Examiner is unable to provide a *prima facie* case of obviousness based on a combination of the references of record and the knowledge generally available in the art, to teach the elements required by at least claim 91 of the instant invention. For this reason, the Examiner's rejection is improper and should be withdrawn.

Although Appellants were not required to do so (because the Examiner has failed to meet the burden of presenting a *prima facie* obviousness rejection), Appellants set forth objective indicia of non-obviousness. This evidence demonstrated an unexpected synergistic effect of the claimed combination which led to surprising results amounting to a 100-fold increase in antiviral activity of the present invention as compared to the antiviral activity of n-docosanol. See application as filed, pages 23-26, and 37 C.F.R. §1.132 affidavits by David Ashley and Robert Kleiman previously submitted on 11/15/2007, attached as Exhibits 3-4 to the Appeal Brief.

Rather than provide countering objective evidence, or even addressing the merits of the evidence, the Examiner chose to set forth arguments based on claimed discrepancies in the labeling of the pages 24-26 of the application as filed, further discussed in Exhibits 3-4 of the Appeal Brief. Specifically, the Examiner argues that K100 is synonymous with n-docosanol, rather than the claimed combination. Essentially, the Examiner maintains that

The declaration merely provides antiviral activity for n-docosanol alone which is a saturated alcohol not within the scope of instant claims which contain unsaturated alcohol, docosenol (C22 saturated alcohol). Thus, no antiviral activity data has been provided for the individual unsaturated alcohol, fatty acid salts, and esters. Accordingly, the data is not convincing with respect to the synergistic effects of the combination of the present invention, since there is no comparison data provided for instant combination with individual unsaturated alcohol, fatty acid salts, and esters. (Examiner's Answer, page 15)

Following the Examiner's logic, pages 24-26 of the application as filed and the supporting 37 C.F.R. § 1.132 Affidavits by Robert Kleiman and David Ashley (Exhibits 3-4 of the Appeal Brief) depict the results of n-docosanol alone. In other words, the Examiner suggests that the 100 fold increase in killing of the HSV-1 Strain 6143 shown in the graph was n-docosanol alone compared to n-docosanol alone, which the Examiner admits are not within the scope of the claims. This is of course utterly ridiculous and not supported by the record in this case.

Appellants have put forth various references made in the application as filed to the "composition of the present invention", which clearly refers to three components: alcohols, wax esters, and salts of fatty acids. *See* application as filed, page 13, lines 1-13. For example, page 11, lines 23-26 of the application as filed clearly refer to the testing of "the composition of the present invention". Page 10, lines 3-page 12, line 22 of the application as filed clearly indicate that components of "the present invention" include "unsaturated wax esters", and hydrolyzed wax esters and "monounsaturated long chain alcohols and salts of long chain fatty acids." Appellants respectfully submit that data relating to concentrations of K100 were provided in Exhibit 1 of Exhibits 5 and 6, which is derived from pages 26-27 of the application as filed.

In summary, where the Examiner does not provide any teaching or reference for the claimed combination, nor any explanation as to how the unexpected, synergistic results of the claimed combination could be predictable, an obviousness rejection cannot be proper. Therefore,

Appellants respectfully maintain their request that the rejections of claims 91-92 under §103 be withdrawn.

ISSUE 2: REJECTIONS UNDER §103(a) OF CLAIMS 93-102

Appellants hereby incorporate and reiterate all arguments/remarks made under the previous section relating to the rejection of claims 91-92 under §103 in this section.

Claims 93-102 are rejected under 35 U.S.C. §103 as purportedly being unpatentable over U.S. Patent No. 5,952,392 to Katz *et al.* in view of PCT Publication No. WO 9602244 A1 to Sintov *et al.*, and further in view of U.S. Patent No. 4,874, 794 to Katz or U.S. Patent No. 5,070,107 to Katz. Appellants further submit that a *prima facie* case of obviousness has not been established, as discussed in Appellants' Appeal Brief, pages 22-24.

In response to the Examiner's arguments, and as discussed above, Appellants maintain that the present invention could not have been deduced from the prior art. Specifically, neither the knowledge in the art, nor any cited reference, taken either alone or in combination, teaches "at least one salt of a jojoba-derived trans-free fatty acid according to the formula $R^1-COO^-M^+$, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12", as required by claim 93 of the present invention. Moreover, the Examiner has provided no evidence to suggest that the claimed elements could be used to provide the synergistic and unexpected anti-viral activity demonstrated in Applicants' invention. See Appeal Brief, Exhibits 5 and 6. That notwithstanding, the Examiner concludes that it would have been obvious to optimize parameters in order to achieve the claimed invention in accordance with *In re Boesch*. (Examiner's Answer, page 17).

Under M.P.E.P. §2144.05, "A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation". Within this context, *In re Boesch* stands for the proposition of optimizing these parameters to receive a beneficial result. Thus, effectively, the Examiner argues step 2 without arguing step 1. That is, the Examiner has not put forth *prima facie* evidence that the claimed fatty acid salts in combination with the claimed long chain alcohols and mixed esters are recognized to produce a

desirable result. In other words, it is *non-sequitur* to argue that optimization of parameters would have been obvious when the parameters were not even identified in the prior art.

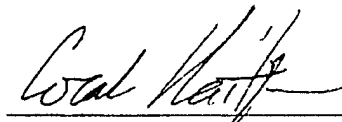
As in the instant case, where the Examiner has not provided any teaching or reference for the claimed combination, nor any explanation as to how the unexpected, synergistic results of the claimed combination could be predicted, an obviousness rejection may not be properly applied. Therefore, Appellants respectfully maintain that the rejections of claims **93-102** under §103 be withdrawn.

CONCLUSION

Appellants therefore respectfully request reversal of the final rejection and the allowance of the subject application.

Respectfully submitted,
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Date: 01/06/2009



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APPENDIX A (CLAIMS APPENDIX)

91. A method for treating at least one of virus-induced and inflammatory diseases, said method comprising the step of providing a topical composition consisting essentially of:

at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula $R^1\text{-COO}^-\text{M}^+$, wherein: R^1 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula $R^2\text{-COO-R}^3$, wherein: R^2 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

92. The method of claim 91, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

93. A method for treating viral infections, said method comprising the step of intravenous delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C₁₈ to C₂₄ monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula R¹-COO⁻M⁺, wherein: R¹ comprises CH₃(CH₂)₇CH=CHCH₂(CH₂)_x; x is at least one of 8, 10, and 12; and M⁺ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula R²-COO-R³, wherein: R² comprises CH₃(CH₂)₇CH=CHCH₂(CH₂)_y; y is at least one of 6, 8, 10 and 12; and R³ is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

94. The method of claim 93, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

95. A method for treating viral infections, said method comprising the step of intramuscular delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C₁₈ to C₂₄ monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula $R^1\text{-COO}^-\text{M}^+$,
wherein: R^1 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_x$; x is at least one of 8, 10, and 12;
and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula $R^2\text{-COO-R}^3$, wherein: R^2 comprises
 $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of
an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

96. The method of claim 95, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

97. A method for treating viral infections, said method comprising the step of trans-mucousal delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula $R^1\text{-COO}^-\text{M}^+$,
wherein: R^1 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_x$; x is at least one of 8, 10, and 12;
and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula $R^2\text{-COO-R}^3$, wherein: R^2 comprises

$\text{CH}_3(\text{CH}_2)_7\text{CH=CHCH}_2(\text{CH}_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

98. The method of claim 97, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

99. A method for treating viral infections, said method comprising the step of transdermal delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one C_{18} to C_{24} monounsaturated alcohol in a physiologically active carrier;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula $\text{R}^1\text{-COO}^-\text{M}^+$, wherein: R^1 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH=CHCH}_2(\text{CH}_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula $\text{R}^2\text{-COO-R}^3$, wherein: R^2 comprises

$\text{CH}_3(\text{CH}_2)_7\text{CH=CHCH}_2(\text{CH}_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

100. The method of claim **99**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.

101. A method for treating viral infections, said method comprising the step of trans-membranal delivery of a composition consisting essentially of:

an effective amount of from about 0.1 mg to about 2 gm per 50 kg of body weight of a compound comprising at least one monounsaturated alcohol having between 18 and 24 carbons in at least one of a physiologically acceptable liquid, cream, gel and suppository carrier into at least one of an anus and vagina of an animal to be treated;

at least one salt of a jojoba-derived trans-free fatty acid according to the formula $R^1\text{-COO}^-\text{M}^+$, wherein: R^1 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and

at least one mixed ester according to the formula $\text{R}^2\text{-COO-R}^3$, wherein: R^2 comprises $\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CHCH}_2(\text{CH}_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms.

102. The method of claim **101**, wherein said composition comprises at least one of: about 1% octadecenol; about 44% eicosenol; about 45% docosenol; and about 9% tetracosenol by total alcohol weight.